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ScienceDirect
Journal of Forensic and Legal Medicine 15 (2008) 37–41
JOURNAL OF FORENSIC AND LEGAL MEDICINE
www.elsevier.com/jflm

Case Report

Silent bony calcification of coronaries in an adolescent – an unusual case

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Received 9 April 2006; received in revised form 11 October 2006; accepted 30 October 2006

Abstract

This is a case report of 16-year-old adolescent school boy who died due to unusual calcification of coronary arteries. He died while cycling with his friends. While cycling fast he fell. He was brought dead to hospital. At times unsuspected cardiac lesions cause sudden death during extraneous physical activities in healthy persons. Sudden death in adolescents is not very common. It is an unusual case as apparently healthy adolescent boy actively participating in sports had stony hard coronary arteries. The coronaries showed advanced calcification and early bone formation. The myocardial septum had extensive fibrosis. The pathogenesis and other possible similar conditions are also discussed in the report.

Keywords: Death in sports; Adolescent sudden death; Unusual calcification of coronaries; Bone formation in coronary arteries

1. Introduction

Atherosclerosis is a disease of elastic and muscular arteries that results in the progressive accumulation of smooth muscle cells, lipids, and extra cellular matrix constituents within intimae. The various complications of atherosclerosis are luminal occlusion, ulceration, dystrophic calcification, haemorrhage, plaque rupture, and aneurysm formation.

Atherosclerotic calcification is an organized, regulated process similar to bone formation that occurs only when other aspects of atherosclerosis are also present.[1] Atherosclerotic calcification begins as early as the second decade of life, just after fatty streak formation.[2]

Calcium phosphate (hydroxyapatite), which contains 40% calcium by weight, precipitates in diseased coronary arteries by a mechanism similar to that found in active bone formation and remodeling.[3] It is analogous to the way matrix vesicles pinch off from chondrocytes in developing bone.[4] It is postulated that vesicles, derived from dead foam and smooth muscle cells debris and contained within extra cellular lipid-rich accumulations, may also serve as the sites of small calcium deposits.[5,6] A very close spatial relationship between cholesterol deposits and hydroxyapaptitie has been demonstrated.[7]

Coronary calcification is not easily detected on chest X-ray. Accuracy is only 42% compared with fluoroscopy, which itself is not extremely sensitive.[3] CT scan is extremely sensitive in detecting coronary calcification.[8] The differential diagnosis of sudden death in young people, mainly include infection, epilepsy, asthma, pulmonary embolism, and intracranial haemorrhage.[6]

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1353-1131/$ - see front matter © 2007 Published by Elsevier Ltd and FFLM.
doi:10.1016/j.jcfm.2006.10.013

2. Case summary

The deceased died suddenly while riding his bicycle with friends in the early morning hours. He had performed some other exercises prior to the ride. He was apparently well without any history of significant medical illness. There was also no history of any other young sudden deaths in the family. Both his maternal as well as paternal relatives did not have any history of major metabolic disorder.

On autopsy examination, the body was that of a well-nourished, well-built adult Chinese male, 174 cm in length and 73 kg in weight. The body was dressed in sports attire i.e. a dark blue jacket and tight black short pants. There were fresh abrasions and bruises over the knees and elbows consistent with a fall. A complete autopsy was conducted.

2.1. Heart

The pericardium was intact and of normal thickness. There was no unusual collection of fluid within the pericardial sac. The great vessels arising from the heart were anatomically normal. The heart weighed 335 g, was of normal configuration, with the four chambers showing concordance. The epicardium and endocardium were unremarkable. The myocardium however showed diffuse whitish, fibrous areas in the interventricular septum and left ventricle (Fig. 1). An area measuring 2.3 cm across showing changes consistent with that of recent infarction was also seen in the left ventricle near the apex. The right and left ventricular walls were of normal thickness.

The left anterior descending coronary artery was dilated and calcified in the proximal 1.5 cm × 1.2 cm (Fig. 2) portion. The dilated and hardened segment of artery was dissected out (Fig. 3a) and histological section shows a distended multi-barrelled lumen due to recanalization (Fig. 3b). All other coronary arteries were patent and showed only mild calcification. The abdominal aorta and other major arteries did not show any obvious atherosclerotic changes. Microphotographs 4a and 4b show bone formation and bony-spicules with advanced atherosclerosis in the wall of left anterior descending artery.

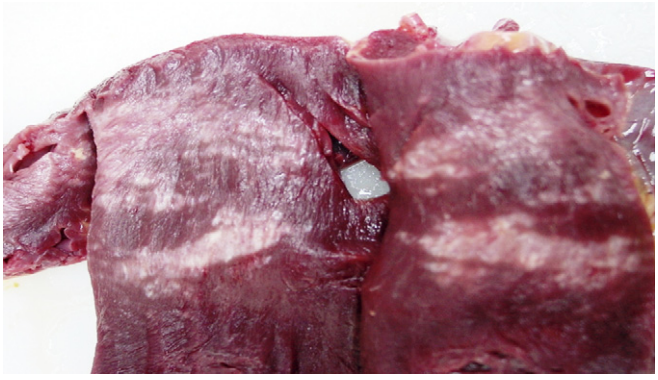

Fig. 1. Gross examination showed diffuse whitish areas of fibrosis in the septum. The myocardium is congested. The empty space is due to the calcified coronary artery, which was removed for histopathological examination.

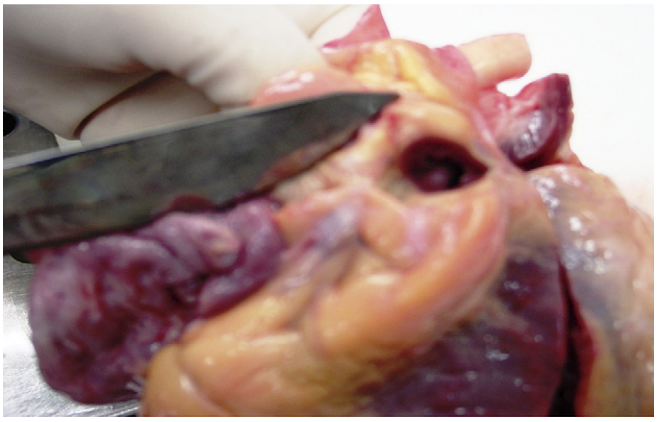

Fig. 2. The proximal part of left anterior descending branch of the left coronary artery showed bulbous dilation, blockage of its lumen and stony hard calcification.

Sections of the heart showed areas of fatty infiltration in representative sections of the right ventricle. The fatty change involved the entire thickness of the ventricular wall and was associated with interstitial fibrosis (Fig. 5a). There were also wide swaths of myocardial fibrosis consistent with areas of old healed infarction (Fig. 5b), as well as areas of recent infarction. Other areas in the heart showed myocardial fatty infiltration, fibrosis and marked myofibrillary disarray (Fig. 5c). The proximal and middle segments of right coronary artery were embedded within myocardium, i.e. bridging. These features were consistent with arrhythmogenic right ventricular dysplasia.

2.2. Airways

The trachea and bronchi contained a small amount of mucus. The lungs (right 605 g, left 560 g) exuded fluid on sectioning due to oedema. Histology showed not only oedema but intra-alveolar haemorrhage (Fig. 5d).

2.3. Endocrine system

The pituitary, thyroid, parathyroid, and adrenal glands were unremarkable.

3. Discussion

Athletes are viewed as the healthiest and most energetic people in our society. Hence sudden deaths in this group invariably cause public concern and anxiety. Sudden deaths in athletes are mainly due to unsuspected cardiovascular diseases.[9–12]

The incidence of sudden death among athletes at high school and college level is one in 200,000.[13,14] In adult athletes, the incidence of sudden death is one in 50,000.[13,14] Causes of sudden death in athletes can be mentioned in decreasing order as hypertrophic cardiomyopathy, coro-

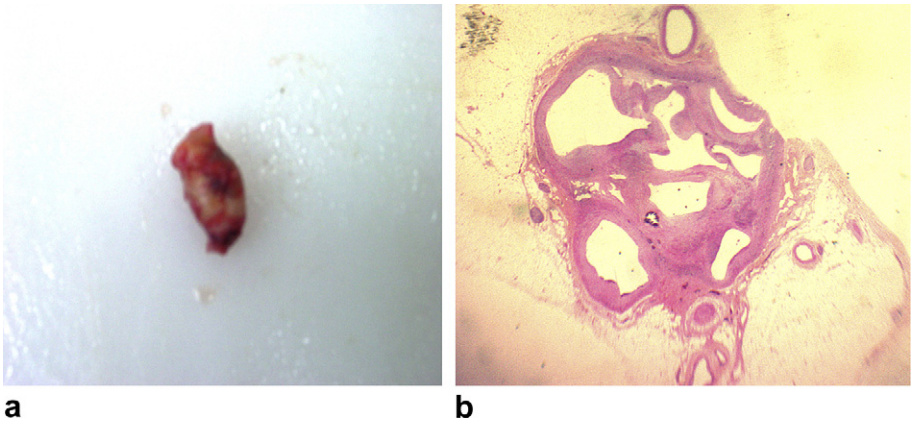

Fig. 3. (a) Segment of atherosclerosed, dilated, calcified and stenosed left anterior descending artery. (b) Cross-sectional view of calcified coronary artery with multiple lumens and atherosclerosis (haematoxylin and eosin, ×5 magnification).

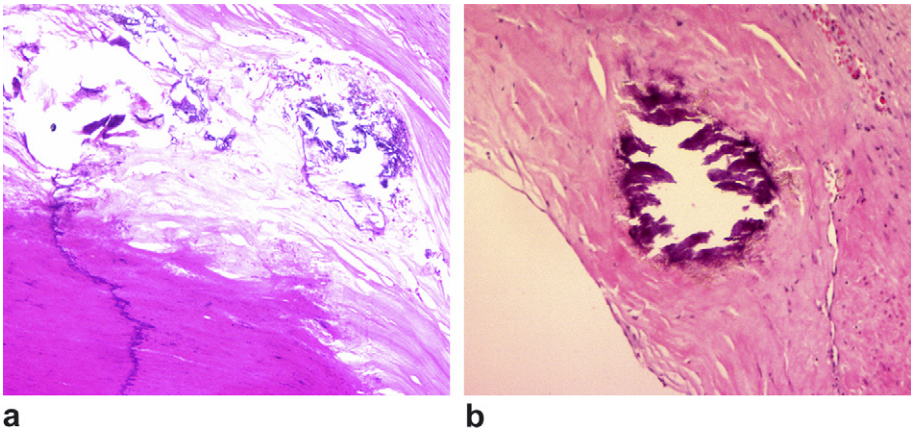

Fig. 4. (a, b) Section of left anterior descending coronary artery showing extensive calcification and changes suggestive of early bone formation (a) (haematoxylin and eosin, ×50 magnification).

nary anomalies, increased cardiac mass, ruptured aorta, tunnel aorta, aortic stenosis, myocarditis, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, mitral valve prolapse, coronary artery disease, and others.[9] The most common cause of sudden death in sports activities still remains coronary artery disease.[14] However, in one study of 269 cases of sudden death during sports, the deaths were due to arrhythmogenic right ventricular cardiomyopathy in 22.4%, coronary atherosclerosis in 18.4%, and anomalous origin of a coronary artery atherosclerosis in 12.2%.[13,14]

A condition that may show similar finding is Takayasu's arteritis. This is an inflammatory disease of unknown origin involving the aorta and its primary branches. The inflammation results in varying degrees of stenosis, occlusion and/or dilation of the involved vessels. The disease may be patchy with normal skip areas in between, or may be diffuse involving the entire length of diseased arteries. Its association with tuberculosis has been described. Coronary artery involvement in Takayasu's arteritis is usually ostial and proximal. It rarely shows diffuse lesions or arteritis with aneurysm.[15] Granulomatous diseases are associated with high levels of calcitriol which is produced by macrophages, the latter a component of granulomata. Calcitriol is a hormone that enhances calcification.[15] In this case, there was diffuse calcification in both coronaries. However, this case did not show any exudative or granulomatous cellular infiltrates.

In hyperparathyroidism, there can be excessive calcification. In fact primary hyperparathyroidism is considered a disease of "stones and bones". Hypercalcaemia in this disorder may remain silent or mild for long periods because some parathyroid adenomas respond to the negative feedback generated by the elevated plasma calcium levels. Increased parathyroid hormone levels lead to hypercalceamia which is directly caused by increased absorption of intestinal calcium. In normal calcium homeostasis, plasma calcium is maintained within the normal reference range by complex interplay of three major hormones, viz parathyroid, 1,25-dihydoxyvitamin D (calcitriol), and calcitonin. Milk alkali syndrome, hypervitaminosis A and D are also associated with increased plasma calcium levels. In this case, the plasma calcium level was within normal reference range.

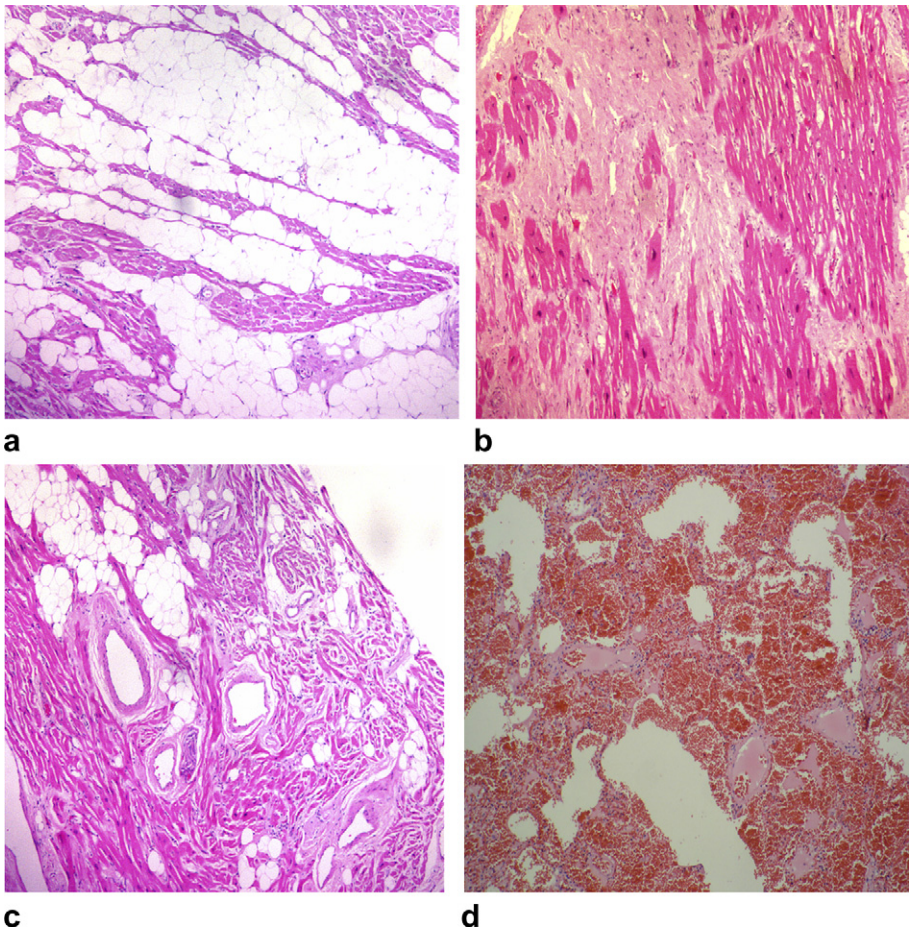

Fig. 5. (a) Myocardium with marked adipose tissue infiltration, and mild focal fibrosis. (b) Myocardium showing area of dense interstitial fibrosis consistent with healed infarction. (c) Myocardium with interstitial fibrosis, fatty infiltration, and marked fibre disarray. (d) Lung showing pulmonary oedema and hemorrhagic changes (haematoxylin and eosin, ×50 magnification).

Increased vessel wall calcification may also be associated with diabetes mellitus, hypertension, chronic renal disease and end stage kidney disease.[16] The protective reparative mechanism of atherosclerosis and non-diabetic atherosclerosis may be rooted in our embryonic genetic memory as part and parcel of our healing process.[16] When atherosclerosis occurs in the small intramural vessels in the heart leading to medial thickening and luminal narrowing, the result may be an increased risk of arrhythmias from the most inconsequential provocation. Other predisposing factors for arrhythmias include left atrial enlargement, severe left ventricular hypertrophy and left ventricular outflow obstruction.[10,17,18]

Sudden cardiac death is defined as unexpected death from cardiac causes, occurring within one hour after onset of symptoms or without any symptoms at all.[19] In the older age group, atherosclerosis of coronary arteries is the main pathological cause. But in the younger age group, other pathologies such as congenital heart abnormalities, valvular diseases, pulmonary hypertension, myocarditis, hereditary or acquired abnormalities in conducting system, cardiomyopathies and isolated hypertrophy of heart due to hypertension or other unknown causes, may result in sudden cardiac deaths.[20]

In this case, the deceased was totally asymptomatic although there was advance calcification of his coronary arteries on autopsy and histopathological examination. Both his parents and his two younger siblings were apparently healthy and similarly asymptomatic. All family members were subsequently examined by the cardiologist and endocrinologist, and were all found to be normal. There was no history of any sudden deaths in both maternal and paternal sides of the family. Silent atherosclerosis with advance focal calcification could not be satisfactorily associated with any other well-established condition in this case. We propose that this may be a new entity altogether or the manifestation of an unusual granulomatous infection or undiagnosed hormonal abnormality, with a chronic relapsing course.

References

1. Lewis Wexler, Bruce Brundage, Crouse John, Robert Detrano, Valentin F, Jamshid M, et al. Coronary calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. *Circulation.* 1996;**94**:1175–92.
2. Stary HC. The sequence of cell and matrix changes in atherosclerotic lesions of coronary arteries in the first forty years of life. *Eur Hear J* 1990;**11**(Suppl. E):3–19.

3. Souza AS, Bream PR, Elliot LP. Chest film detection of coronary artery calcification: the value of the CAC triangle. *Radiology.* 1978;**129**:7–10.
4. Bostrom K, Watson KE, Horn S, Wortham C, Herman IM, Demer LL. Bone morphogenetic protein expression in human atherosclerotic aorta. *J Clin Invest* 1993;**91**:1800–9.
5. Tanimura A, McGregor DH, Anderson HC. Calcification in atherosclerosis, I: human studies. *J Exp Pathol* 1986;**2**:275–97.
6. Stary HC. Composition and classification of human atherosclerotic lesions. *Virchows Arch A Pathol Anat Histopathol* 1992;**421**:277–90.
7. Starry HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis: a report from the Committee on Vascular Lesions of the Council on Atherosclerosis, American Heart Assoc. *Circulation.* 1995;**92**:1355–74.
8. Hirsch D, Azoury R, Sarig S, Kruth HS. Localization of cholesterol and hydroxyapaptite in human atherosclerotic lesions calcification. *Tissue Int* 1993;**52**:94–8.
9. Maron BJ, Thompson PD, Puffer JC. Recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. 26th Bethesda Conference. *J Am Coll Cardiol* 1994;**24**:845–99.
10. Olivotto I, Cecchi F, Casey SA, Dolara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiac myopathy. *Circulation.* 2001;**104**:2517–24.
11. Maron BJ, Olivotto I, Bellone P, Conte MR, Cecchi F, Flygening P, Carey Susan, et al. Clinical Profile of stroke in 900 patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;**39**:301–7.
12. Morentin B, Paz Suarej, Mier M. Incidence and causes of sudden death in persons less than 36 years of age. *Med Clin (Berc)* 2001;**116**(8):281–5.
13. Watts EJ. Deaths due to coronary heart disease during sport. *BMJ.* 1994;**309**:1304.
14. Hillis WS, Mclatyre PD, MacLean J, Goodwin JF, McKenna J. ABC of sports medicine: sudden death in sport. *BMJ.* 1994;**309**:657–60.
15. Kothari SS. Takayasu's arteritis in children – a review. *Images Paediatric Cardiol* 2002;**9**:4–23.
16. Demur LL. A skeleton in the atherosclerosis closet. *Circulation.* 1995;**92**:2029–32.
17. Basso C et al. Cardiovascular causes of sudden death in young individuals including athletes. *Cardiol Rev* 1999;**7**(3):127–35.
18. Burke AP, Farb A, Virmani R, Goodin J, Smialek JE. Sports related and non-sports related sudden cardiac death in young adults. *Am Heart J* 1991;**121**:568–75.
19. Wever EFD, Hauer RNW, Oomen A, Peters RHJ, Bakker PFA, Robles de Medina EO. Unfavorable outcome in patients with primary electrical disease who survived an episode of ventricular fibrillation. *Circulation.* 1993;**88**:1021–9.
20. Kumar V, Abbas AK, Fausto N. *Robbins and Cotran pathologic basis of disease*, vol. 743. 7th ed. Saunders; 2005. p. 586–601.